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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,578	01/17/2002	James E. Rothman	11746/46003	9899

26646 7590 03/31/2005

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EXAMINER	
CHANDRA, GYAN	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,578	ROTHMAN ET AL.	
	Examiner	Art Unit	
	Gyan Chandra	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/12/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Election/Restrictions

This application is a divisional of US Application No. 08/961,707.

Status of Application, Amendments, And/Or Claims

Claims 14-30 are canceled.

Claims 1-13 are pending and under examination.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

The reference "WO 97/06281" should be "WO 97/06821".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Blond-Elguindi et.al. (IDS, Cell 75:717-728, 1993).

Claimed invention is drawn to a method of identifying a peptide which binds to a heat shock protein comprising (i) contacting a phage display library comprising a plurality of bacteriophage expressing a surface protein, a plurality of inserted peptide with a HSP target in a physiologic binding buffer with ionic strength of an aqueous solution of 100-150 mM NaCl and comprises a non hydrolyzable nucleotide, (ii) isolation of a phage that binds to a HSP target, and (iii) identification of the inserted peptide expressed in the surface protein of the phage.

Blond-Elguindi et.al. teach isolation and identification of a heat shock protein BiP, which is a member of heat shock protein-70 (HSP70) family present in the endoplasmic reticulum of eukaryotic cells (page 717, 1st paragraph of the left column). They teach isolation and identification of a peptide using a bacteriophage library expressing a plurality of peptides at the N-terminus of an adsorption protein in a binding buffer that comprises phosphate buffer saline (PBS) that contains NaCl 133 mM (Blond-Elguindi et.al, JBC 268, 12730-12735, 1993). They also teach use of a non hydrolyzable nucleotide, ATP in PBS for the elution of bacteriophage.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blond-Elguindi et.al. (IDS, Cell 75:717-728, 1993) in view of Suzuki et.al. (The J. Cell Biol. 14: 189-205, 1991).

Claimed invention is drawn to a method of identifying a peptide which binds to a heat shock protein comprising contacting a phage display library comprising a plurality of bacteriophage expressing a surface protein in a binding buffer wherein the binding buffer comprises calcium ion at a concentration of 1-25 millimolar.

The teachings of Blond-Elguindi et al. are summarized as set forth supra. Blond-Elguindi et.al. do not teach use of CaCl2 in the binding buffer. Suzuki et al. teach that the level of calcium serves to modulate the association and dissociation of heat shock proteins within endoplasmic reticulum. High levels calcium ions help binding of newly

synthesized protein to a heat shock protein (page, 190 end of the first paragraph of the left column). They teach ca2+ levels can vary through out ER using calcium ionophore, A23187. Further, they treat cells with a 20 mM CaCl2 to overcome with the ionophore A23187 impact suggesting that 20 mM level would help in protein binding (page 200, bridging paragraph), which meets the limitation of the claimed invention of a binding buffer comprising 1-25 mM CaCl2.

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to include CaCl2 in the binding buffer of Blond-Elguindi et.al. because Suzuki et al suggest that the level of calcium can modulate binding with a HSP. The person of ordinary skill in the art would have been motivated do so with a reasonable level of success because Suzuki et al teach a high level calcium would help binding of proteins with a heat shock protein.

Claims 1-2, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blond-Elguindi et.al. (IDS, Cell 75:717-728, 1993) in view of Kay et.al (US Patent No. 5,498538).

Claimed invention is drawn to a method of identifying a peptide which binds to a heat shock protein comprising contacting a phage display library comprising a plurality of bacteriophage expressing a surface protein in a binding buffer wherein the binding buffer comprises a reducing agent.

The teachings of Blond-Elguindi et al is summarized as set forth supra. Blond-Elguindi et.al. do not teach use of a reducing agent in the binding buffer. Kay et.al.

teach that reducing agent such as DTT or mercaptoethanol helps in minimizing unpaired cysteine residue from binding vectors (column 19, lines 1-10).

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to include a reducing agent in the binding buffer as taught by Blond-Elguindi et al, as evident from figure-6 a number of peptides having cysteine residues, to help maintain unpaired cysteine residue in reduced form and not allowing any non specific binding with the vector DNA as taught by Kay et al. The person of ordinary skill in the art would have been motivated do so with a reasonable level of success because Kay et.al. teach that reducing agents help unpaired cysteine residue in reduced form to minimize binding of a peptide with the vector DNA.

Claims 6-10, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blond-Elguindi et.al. (IDS, Cell 75:717-728, 1993) in view of Whitesell et.al. (IDS, Proc. Natl. Acad. Sci. 91: 8324-8328).

Claimed invention is drawn to a method of identifying a peptide which binds to a heat shock protein comprising (i) contacting a phage display library comprising a plurality of bacteriophage expressing a surface protein, a plurality of inserted peptide with a HSP target bound to a benzoquinone ansamycin antibiotic wherein a benzoquinone ansamycin is herbimycin A or geldanmycin, (ii) isolation of a phage that binds to a HSP target, and (iii) identification of the inserted peptide expressed in the surface protein of the phage.

The teachings of Blond-Elguindi et.al. is summarized as set forth supra. Blond-Elguindi et.al. do not teach a HSP target bound to a benzoquinone ansamycin antibiotic. Whitsell et.al. teach the putative tyrosine kinase inhibitors geldanamycin (GA) and herbinmycin A (HA) revert the morphology of fibroblasts transformed by many oncogenic tyrosine kinases. They suggest that the ability to revert the transformed phenotype may be due to a direct binding of HA or GA with a heat shock protein HSP90.

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to insert a peptide with a HSP target bound to a benzoquinone ansamycin such as herbimycin A or geldanmycin and screen a bacteriophage library to isolate and identify a peptide that binds to HA or GA as taught by Blond-Elguindi et al as art recognizes role that is played by antibiotics such as geldanamycin (GA) and herbinmycin A (HA) in reversal of fibroblast morphology. The person of ordinary skill in the art would have been motivated do so with a reasonable level of success because Whitesell et al teach that herbimycin A or geldanmycin binds to a heat shock protein HSP90.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blond-Elguindi et.al in view of Whitesell et.al. as applied to claims 6-10 and 13 above, and further in view of Suzuki et.al. (The J. Cell Biol. 14: 189-205, 1991).

Claimed invention is drawn to a method of identifying a peptide which binds to a heat shock protein comprising contacting a phage display library comprising a plurality of bacteriophage expressing a surface protein, a plurality of inserted peptide with a hsp

target bound to a benzoquinone ansamycin antibiotic wherein a benzoquinone ansamycin is herbimycin A or geldanmycin and binding buffer comprises calcium ion at a concentration of 1-25 micromolar.

The teachings of Blond-Elguindi et al in combination to Whitesell et al are summerized as set forth supra. . Blond-Elguindi et.al. and Whitesell et al do not teach use of CaCl2 in their binding buffer. Suzuki et al. teach that the level of calcium serves to modulate the association and dissociation of heat shock proteins within endoplasimic reticulum. Suzuki et al. teach that lower level of calcium helps releasing protein bound with a heat shock protein. A heat shock protein bound with a target bound with an antibiotic such as a benzoquinone ansamycin is herbimycin A or geldanmycin would need a lower calcium ion in the binding buffer to avoid co-precipitation as Suzuki et al show that the presence of ATP helps in coprecipitated proteins (page 193, left column). They used Ca2+ in 1-100 micromollar range to avoid precipitation upto 80%. Therefore, the presence of 1-100 micromolar calcium in a binding buffer for identifying a peptide that binds to a HSP using a phage display library would minimize a heat shock protein from precipitating during the peptide identification and isolation process.

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to include CaCl2 in the binding buffer of Blond-Elguindi et.al in combination of Whitesell et.al. because Suzuki et al suggest that the level of calcium can modulate binding with a HSP. The person of ordinary skill in the art would have been motivated do so with a reasonable level of success because Suzuki et al

teach the presence of calcium ion in the binding buffer would minimize precipitation during the binding of a peptide with a heat shock protein.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Blond-Elguindi et.al in view of Whitesell et.al. as applied to claims 6-10 and 13 above, and further in view of Kay et.al (US Patent No. 5,498538).

The teachings of Blond-Elguindi et al in combination to Whitesell et al are summarized as set forth supra. Blond-Elguindi et.al. and Whitesell et al do not teach use of a reducing agent in the binding buffer. Kay et.al. teach that reducing agent such as DTT or mercaptoethanol helps in minimizing unpaired cysteine residue from binding vectors (column 19, lines 1-10).

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to include a reducing agent in the binding buffer as taught by Blond-Elguindi et.al in combination of Whitesell et.al. to help maintain unpaired cysteine residue in reduced form and not allowing any non specific binding with the vector DNA as taught by Kay et al. The person of ordinary skill in the art would have been motivated do so with a reasonable level of success because Kay et.al. teach that reducing agents help unpaired cysteine residue in reduced form and minimizes binding of a peptide with the vector DNA.

Conclusion

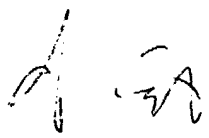
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gyan Chandra
AU 1646
14 March 2005



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